

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To: Received/Empfangen
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Dat: 01. Okt. 2004

Ref:

Frist: 1.2.05 (F)

NOTIFICATION OF TRANSMITTAL OF
 THE INTERNATIONAL SEARCH REPORT AND
 THE WRITTEN OPINION OF THE INTERNATIONAL
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

| | |
|--|--|
| Applicant's or agent's file reference 7954 PCT | Date of mailing (day/month/year) 01/10/2004 |
| International application No. PCT/CH2004/000405 | FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date (day/month/year) 28/06/2004 |
| Applicant MAX ZELLER SOHNE AG | |

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders


Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

| | |
|--|------------------------------------|
| Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Authorized officer Eva Boháčová |
|--|------------------------------------|

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CH2004/000405

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K35/78 A61P15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X D1a | WO 03/000074 A (SAKAI YASUSHI ; YOKOO YOSHIHARU (JP); KYOWA HAKKO KOGYO KK (JP)) 3 January 2003 (2003-01-03) see following English language equivalent | 1-4,6 |
| P,X 1b | -& EP 1 407 679 A (KYOWA HAKKO KOGYO KK) 14 April 2004 (2004-04-14) paragraph '0050!; examples 1-7 comparative examples 1-4 | 1-4,6 |
| X D2 | WO 03/037096 A (GREENE JOHN BERTRAM ; BRIGHTWATER HORTICULTURE LTD (NZ)) 8 May 2003 (2003-05-08) page 5, line 26 - line 30; examples 1,2 | 1-4,6 |
| X D3 | WO 02/067962 A (LI HONGKE ; LIU DAYOU (CN); LIU DATONG (CN); LIU YIFENG (CN); QIU JINW) 6 September 2002 (2002-09-06) see following English language equivalent -/-- | 1-4,6 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

17 September 2004

Date of mailing of the international search report

01/10/2004

Name and mailing address of the ISA :

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Pilling, S

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| P, X D3 | -& US 2004/067263 A1 (LI HONGKE ET AL) 8 April 2004 (2004-04-08) example 1 | 1-4,6 D3 |
| X D4 | WO 02/30436 A (KREUTER MATTHIAS HEINRICH ; TITTEL GEROLF (DE); CMI AG (DE); WAGNER HI) 18 April 2002 (2002-04-18) example 1 | 1-4,6 D4 |
| X D5 | EP 0 324 197 A (LINNEA SA) 19 July 1989 (1989-07-19) example 1 | 1-4,6 D5 |
| X D6 | US 2003/054050 A1 (HOFFMANN DAVID LUDWIG ET AL) 20 March 2003 (2003-03-20) paragraph '0083! - paragraph '0085! | 1-4,6 D6 |
| X D7 | US 4 985 247 A (LIU YAGUANG) 15 January 1991 (1991-01-15) examples 1,6 | 1-4,6 D-7 |
| X D8 | WO 01/05415 A (BRUENNER NILS ; KOEBENHAVNS UNI (DK); SPANG THOMSEN MOGENS (DK)) 25 January 2001 (2001-01-25) cited in the application page 11, line 10 - page 12, line 8 | 7-10 D8 |
| X D9 | LISKE E: "Therapeutic Efficacy and Safety of Cimicifuga racemosa for Gynecologic Disorders" ADVANCES IN THERAPY, HEALTH COMMUNICATIONS, METUCHEN, NJ, US, vol. 15, no. 1, 1998, pages 45-53, XP001068814 ISSN: 0741-238X abstract page 46, line 27 - line 30 | 7-10 D9 |
| X D10 | ZHENG Q Y ET AL: "Chapter 33: CIMIPURE (CIMICIFUGA RACEMOSA): A STANDARDIZED BLACK COHOSH EXTRACT WITH NOVEL TRITERPENE GLYCOSIDE FOR MENOPAUSAL WOMEN" PHYTOCHEMICALS AND PHYTOPHARMACEUTICALS, XX, XX, 2000, pages 360-370, XP001069523 page 370 | 7-10 D-10 |
| X D11 | PATENT ABSTRACTS OF JAPAN vol. 1997, no. 06, 30 June 1997 (1997-06-30) & JP 9 030977 A (NANBA TSUNEO; KADOTA SHIGETOSHI; KAKEN PHARMACEUT CO LTD), 4 February 1997 (1997-02-04) abstract | 7-10 D-11 |
| | -/-- | |

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CH2004/000405

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X D-12 | DATABASE WPI Section Ch, Week 198411 Derwent Publications Ltd., London, GB; Class B04, AN 1984-065078 XP002296802 & JP 59 020298 A (SUNTORY LTD) 1 February 1984 (1984-02-01) abstract | 7-10 D-12 |
| X D-13 | BORRELLI F ET AL: "Cimicifuga racemosa: A systematic review of its clinical efficacy" EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, SPRINGER VERLAG, DE, vol. 58, no. 4, July 2002 (2002-07), pages 235-241, XP002237716 ISSN: 0031-6970 Introduction and Discussion | 7-10 D-13 |
| X D-14 | US 6 267 994 B1 (FREUDENSTEIN JOHANNES ET AL) 31 July 2001 (2001-07-31) cited in the application column 4, line 34 - line 41 | 7-10 D-14 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CH2004/000405

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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| WO 03000074 | A | 03-01-2003 | CA 2451144 A1 EP 1407679 A1 WO 03000074 A1 US 2004161524 A1 | 03-01-2003 14-04-2004 03-01-2003 19-08-2004 |
| EP 1407679 | A | 14-04-2004 | CA 2451144 A1 EP 1407679 A1 US 2004161524 A1 WO 03000074 A1 | 03-01-2003 14-04-2004 19-08-2004 03-01-2003 |
| WO 03037096 | A | 08-05-2003 | NZ 515182 A WO 03037096 A1 | 26-03-2004 08-05-2003 |
| WO 02067962 | A | 06-09-2002 | CN 1312253 A WO 02067962 A1 JP 2004518751 T US 2004067263 A1 | 12-09-2001 06-09-2002 24-06-2004 08-04-2004 |
| US 2004067263 | A1 | 08-04-2004 | CN 1312253 A WO 02067962 A1 JP 2004518751 T | 12-09-2001 06-09-2002 24-06-2004 |
| WO 0230436 | A | 18-04-2002 | AU 1399602 A AU 2059402 A CA 2424869 A1 CA 2424930 A1 WO 0228403 A1 WO 0230436 A1 EP 1326624 A1 EP 1333848 A1 JP 2004513092 T JP 2004510822 T US 2004161477 A1 US 2004033275 A1 | 22-04-2002 15-04-2002 11-04-2002 04-04-2003 11-04-2002 18-04-2002 16-07-2003 13-08-2003 30-04-2004 08-04-2004 19-08-2004 19-02-2004 |
| EP 0324197 | A | 19-07-1989 | CH 678150 A5 AR 240020 A1 AT 73343 T DE 3869111 D1 EP 0324197 A1 ES 2030498 T3 GR 3004878 T3 JP 1199989 A JP 2661998 B2 KR 133920 B1 | 15-08-1991 31-01-1990 15-03-1992 16-04-1992 19-07-1989 01-11-1992 28-04-1993 11-08-1989 08-10-1997 22-04-1998 |
| US 2003054050 | A1 | 20-03-2003 | CA 2460203 A1 EP 1446135 A1 WO 03024470 A1 | 27-03-2003 18-08-2004 27-03-2003 |
| US 4985247 | A | 15-01-1991 | US 4886666 A US 4944946 A US 4944945 A | 12-12-1989 31-07-1990 31-07-1990 |
| WO 0105415 | A | 25-01-2001 | AU 771581 B2 AU 5966900 A WO 0105415 A2 EP 1200107 A2 | 25-03-2004 05-02-2001 25-01-2001 02-05-2002 |

INTERNATIONAL SEARCH REPORT

Information on patent family members.

International Application No

PCT/CH2004/000405

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication date |
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| JP 9030977 | A | 04-02-1997 | NONE | | |
| JP 59020298 | A | 01-02-1984 | NONE | | |
| US 6267994 | B1 | 31-07-2001 | DE | 19652183 C1 | 12-02-1998 |
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| | | | AU | 730372 B2 | 08-03-2001 |
| | | | AU | 4830097 A | 18-06-1998 |
| | | | AU | 5549098 A | 15-07-1998 |
| | | | CA | 2245890 A1 | 25-06-1998 |
| | | | WO | 9826791 A1 | 25-06-1998 |
| | | | DE | 59704654 D1 | 25-10-2001 |
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| | | | HU | 9901360 A2 | 30-08-1999 |
| | | | IL | 125776 A | 10-12-2003 |
| | | | NO | 975858 A | 15-06-1998 |
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CH2004/000405

International filing date (day/month/year)
28.06.2004

Priority date (day/month/year)
01.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K35/78, A61P15/12

Applicant
MAX ZELLER SOHNE AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Authorized Officer

Pilling, S

Telephone No. +49 89 2399-8461



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CH2004/000405

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CH2004/000405

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|----------|
| Novelty (N) | Yes: Claims | 5 |
| | No: Claims | 1-4,6-10 |
| Inventive step (IS) | Yes: Claims | 5 |
| | No: Claims | 1-4,6-10 |
| Industrial applicability (IA) | Yes: Claims | 1-10 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D14 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

Claims 1 to 6

2. As indicated herein below (see Item VIII) the definition in Claim 1 of a "*physiologically inert solution mediator*" (PISM) is considered to be vague and unclear. Since, an unclear term cannot be relied upon as a novelty conferring feature this term has been construed to include any substance which is present in an extraction liquid in addition to a single solvent and material extracted from a plant. The following cited documents disclose extraction liquids comprising the following substances present in the extraction liquid in addition to a single solvent and material extracted from a plant;

D1-plant powder such as "*powder of Hydrangeae Dulcis Folium*"- it is clearly disclosed in this document that the addition of the plant powder prevented deposition of the concentrated extract on the wall of a concentration vessel (see paragraph 50, Examples 1 to 7 and Comparative Examples 1 to 4)

D2-citric acid and/or ascorbic acid (see Examples 1 and 2 and page 5 lines 26 to 30 and cf the description of "tartaric acid" as a PISM on present page 5 line 11)

D3-gelatin (see Example 1 and cf the definition of "organic polymer" in present Claim 3)

D4-a mixture of components including water, ethanol, tragacanth gum, maltodextrin (see Example 1 and cf the definition of maltodextrin as a PISM on present page 5 line 10)

D5-celite (diatomaceous earth), butanone and ammonium sulphate (see Example 1)

- D6 (see paragraphs 83-85) and D7 (see Examples 1 and 6) -ethanol or water
3. Thus, it is considered that methods defined in Claims 1 to 4 and 6 are not new in view of the disclosures of each of documents D1 to D7 (Article 33(2) PCT).
 4. None of the documents appears to disclose the subject matter of Claim 5. Thus, the subject matter of Claim 5 is new (Article 33(2) PCT).
 5. The closest prior art in respect of Claim 5 appears to be document D1 since as indicated above, this document teaches that the addition of a plant powder such as "*powder of Hydrangeae Dulcis Folium*" to a plant extract prevents deposition of the concentrated extract on the wall of a concentration vessel. Thus, the difference between the disclosure of document D1 and the subject matter of the present invention is the use of polyvinylpyrrolidone (PVP) as the PISM. Since there is no data concerning the comparative technical effects of plant powder versus PVP, the objective technical problem to be solved in respect of the present invention appears to be "how to find alternative ways of preventing agglomeration and subsequent precipitation of less soluble components of the primary extract upon concentration" (see present page 4 lines 24 to 28 and the present examples establish the technical effects of PVP). The present solution of using PVP does not appear to be obviously derivable from document D1. The IPEA does not believe that plant powder and PVP would not normally be recognised as functionally equivalent for the present purpose. There is no teaching in the presently available prior art document toward the use of PVP to prevent agglomeration/precipitation of any plant extracts.
 6. Thus, the subject matter of Claim 5 is inventive (Article 33(3) PCT).
 7. It may further be helpful to note in this regard, that in view of the fact that the present experimental evidence only establishes the efficacy of PVP that the above finding of inventive step would not be applicable to the further PISMs described on page 5 lines 8 to 12.

Claims 7 to 10

8. A product is not rendered novel merely by virtue of the fact that it is produced by means of a new process. Hence, Claim 7 to 10 are considered to simply define

extracts of *Cimifuga racemosa* and medicaments comprising such extracts. Since documents D8 to D14 already describe such extracts and medicaments, it is considered that the subject matter of Claims 7 to 10 is not new in view of the disclosures of these documents (Article 33(2) PCT).

Re Item VIII

Certain observations on the international application

9. The definition in Claim 1 of a "*physiologically inert solution mediator*" (PISM) is vague and unclear (Article 6 PCT). This term is not a standard term in the present art nor is there any further definition in either the description or the claims of which compounds are included within the scope of this definition and which are excluded. The description only provides a diverse list of further compounds which have not been shown to have any efficacy in solving the present technical problem, *i.e.* preventing agglomeration and subsequent precipitation of less soluble components of the primary extract upon concentration. Moreover this list of compounds includes compounds such as fructose and tartaric acid that would not reasonably be regarded as physiologically inert.